

REMARKS

Claims 1, 2, 4, 42 and 43 stand rejected, and claims 5-14 are objected to. Applicant has amended claim 42 to recite that the polypeptide fragment is at least 258 amino acids in length. Support for this amendment can be found in Applicant's specification at, for example, page 9, lines 16-25, which disclose that a costimulatory molecule can have a variant amino acid sequence from, e.g., amino acid residue 32 to amino acid residue 290 of SEQ ID NO:3 or SEQ ID NO:4. Such a polypeptide thus would have a sequence of 258 amino acids. As such, no new matter has been added.

In light of the above amendment and the following remarks, Applicant respectfully requests reconsideration and allowance of claims 1, 2, 4-14, 42, and 43. Applicant further requests rejoinder and allowance of claims 35-41 and 44-50.

Claim Objections

Claims 5-14 are objected to as being dependent upon a rejected base claim. The Examiner stated that claims 5-14 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In view of the remarks presented herein, Applicant has not amended claims 5-14.

Rejections under 35 U.S.C. §112

The Examiner rejected claims 1, 2, and 4 under 35 U.S.C. §112, first paragraph, for alleged lack on enablement. The Examiner alleged that while the claims recite a genus of polypeptides defined as "variants" of a reference sequence and having reduced binding affinity for PD-1, the specification discloses only a limited number of such variants. The Examiner further asserted that it is unpredictable whether variants other than those having the specifically disclosed amino acid substitutions would retain the required functional activity, and that there is insufficient guidance to direct the skilled artisan as to such functional sequences. The Examiner thus alleged that "the skilled artisan would not reasonably expect the generically recited 'variants' to possess the required functions," and that "the instant claim language does not allow

the skilled artisan to make and use the variant polypeptides commensurate in scope with the instant claims without undue experimentation.

Applicant respectfully disagrees. Present claims 1, 2, and 4 are fully enabled. This is particularly true given that Applicant's specification discloses methods for making variant B7-H1 polypeptides and testing their binding affinity for PD-1. See, for example, the specification at page 25, lines 12-22, and page 26, line 20 to page 28, line 15, which describe methods for making B7-H1 Ig fusion polypeptides, methods for mutagenizing such polypeptides, and methods for using ELISA, FACS, and surface plasmon resonance techniques to evaluate the binding affinity of such polypeptides for PD-1. Such methods were routine and certainly well within the level of skill in the art at the time of Applicant's 2002 priority date, and could have been carried out with no undue experimentation.

Further, Figure 9 of Applicant's specification provides an alignment of the mouse and human B7-H1 amino acid sequences (SEQ ID NOS: 3 and 4, respectively). This alignment shows that the amino acids implicated in binding to PD-1 are conserved between the mouse and human proteins. Specifically, the tyrosine at position 37, the phenylalanine at position 67, the isoleucine at position 115, the lysine at position 124, and the isoleucine at position 126, all of which are important for binding to PD-1 as indicated in Table 1 of the specification, are entirely conserved between mouse and human B7-H1. Thus, a person of skill in the art would have been able to review the alignment shown in Figure 9 to ascertain which positions of B7-H1 are conserved and thus might be likely to be involved in PD-1 binding. No undue experimentation would have been required for such a person to identify a conserved amino acid, mutate that amino acid (e.g., to alanine, serine, or tyrosine as denoted in Table 1), and test the binding affinity of the resulting variant polypeptide for PD-1. Thus, Applicant's specification provides ample guidance for making and using the presently recited polypeptides.

Applicant respectfully notes that the Court has stated that "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (*In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), citing *In re Jackson*, 217 USPQ at 807 (Bd. App. 1982)). In fact, while holding that claims to poxvirus vaccines were enabled, the Federal Circuit cited and agreed with the Board of

Patent Appeals and Interference's observation that "the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary in the field of vaccine preparation." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006). Applicant acknowledges that expenditures of some time and effort also may have been required to make and use the presently claimed variant polypeptides as of the 2002 priority date. As with vaccine preparation, however, such expenditures would have been ordinary and expected in the field of variant polypeptides. Given this fact, particularly in view of the guidance provided by Applicant's specification as described above, it is clear that the present claims are fully enabled.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 1, 2, and 4 under 35 U.S.C. §112, first paragraph.

The Examiner rejected claims 42 and 43 under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. The Examiner alleged that in the absence of a limitation specifying a minimal size for the recited fragments, the specification does not provide an enabling description of polypeptide fragments comprising the specified amino acids of SEQ ID NO:4, wherein the fragments inhibit binding of murine B7-H1 to murine PD-1.

Applicant respectfully disagrees. For at least the reasons cited in Applicant's filings of July 21, 2006 and November 10, 2006, no undue experimentation would have been required for a person of skill in the art to make and use the polypeptide fragments recited in previous claims 42 and 43. Nevertheless, in an attempt to further prosecution, Applicant has amended claim 42 to recite that the polypeptide is at least 258 amino acids in length. Thus, the claims recite a minimal size for the fragments. As such, present claims 42 and 43 are fully enabled.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 42 and 43 under 35 U.S.C. §112, first paragraph.

Request for Rejoinder

Applicant respectfully requests rejoinder of claims 35-41 and 44-50. If an elected claim directed to a product is found allowable, withdrawn process claims that depend from or

otherwise require all the limitations of the allowable product claim will be considered for rejoinder. M.P.E.P. § 821.04(b). Claims 35-41 recite a method for using the purified variant costimulatory polypeptide recited in claim 1, while claims 44-50 recite a method for using the polypeptide fragment recited in claim 42. Thus, claims 35-41 and 44-50 require all the limitations of claims 1 and 42, respectively. Given the amendments and remarks presented here, claims 1 and 42 are in condition for allowance. As such, rejoinder of claims 35-41 and 44-50 is respectfully requested

CONCLUSION

Applicant submits that claims 1, 2, 4-14, 42 and 43 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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